CAUSE NO. 2001-61352

BAYLOR COLLEGE OF MEDICINE and BCM TECHNOLOGIES, INC.	(	IN THE DISTRICT COURT OF
Vs.	(	
CLONTECH LABORATORIES, INC.	(	HARRIS COUNTY, T E X A S
VS.	(	
INVITROGEN CORPORATION	(	133RD JUDICIAL DISTRICT

****

ORAL DEPOSITION OF
STEPHEN ELLEDGE, Ph.D.
MARCH 26, 2003

****

Reported by: LINDA RAYBURN
Job No. 40456

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* * * * *

ORAL DEPOSITION OF STEPHEN ELLEDGE Ph.D., produced as a witness at the instance of the DEFENDANT/COUNTERCLAIM PLAINTIFF, and duly sworn, was taken in the above-styled and numbered cause on MARCH 26, 2003, from 9:04 a.m. to 11:20 a.m., before Linda Rayburn, CSR in and for the State of Texas, reported at Baylor College of Medicine, 1 Baylor Plaza, Cullen Building, Suite 106-A, Houston, Texas, pursuant to the Texas Rules of Civil Procedure and the provisions stated in the record or attached hereto.

A P P E A R A N C E S

FOR THE PLAINTIFF/COUNTERCLAIM DEFENDANT:

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MS. MICHELLE MULLER
Vinson & Elkins
The Terrace 7
2801 Via Fortuna, Suite 100
Austin, Texas 78746

-AND-

MR. PATRICK TURLEY
Baylor College of Medicine
General Counsel Office
1 Baylor Plaza
Houston, Texas 77002

FOR THE DEFENDANTS/COUNTERCLAIM PLAINTIFF:

MR. MARC R. LABGOLD
Patton Boggs, LLP
8484 Westpark Drive, Suite 900

of the Univector system.

Q And in fact, all of the elements of the Univector system, and take it in unconnected form, were all known in the prior art, correct?

A It depends on what you mean by "elements." I don't know what you mean, so perhaps you could define that for me, because it's a very vague term.

Q Why don't you tell me what makes up the Univector system.

MR. BLANKE: Objection, form.

Q (By Mr. Labgold) Or why don't you -- I'll make it a little more defined. What do you consider to be the essential elements of the Univector system?

MR. BLANKE: Objection, form.

THE WITNESS: I consider the essential elements of the Univector system to be the ability to cause the fusion between two molecules using site-specific recombination, one of those molecules being a recipient vector, the other being a donor vector that contains site-specific recombination site, a drug marker and the absence of a functional origin under certain conditions --

Q And --

A The ability to select for that event.

Q Now, the prior art taught site-specific

recombination, correct?

A That is correct.

Q And the prior art taught the use of lox sites for site-specific recombination, correct?

A That is correct.

Q And the prior art taught Cre-mediated recombination using the lox sites?

A That is correct.

Q And the prior art taught drug resistance markers, right?

A Correct.

Q And the prior art taught conditional origins of replication, correct?

A Correct.

Q And the prior art, one that you didn't mention here, but I think is also important to the system, correct me if I'm wrong, the prior art taught cells which would allow for the selection of the conditional origin of replication, correct?

A That is correct.

Q So --

A And also, I would add, I don't know, "element" is a -- I mean, there is also the concept of the purpose of making the fusion event to create expression vectors and things like that. That was a novel element.

Q Well, expression vectors were known before, correct?

A Right. But I think the use of site-specific recombination in this way wasn't appreciated, so that that I think is a novel element, because without the need to do that, there would be no coming together of the other elements.

Q But prior to your invention, people clearly desired and actually accomplished the ability to subclone pieces of DNA from one vector to another, correct?

A Yes, using conventional methods.

Q And some of those conventional methods would be what I would refer to as kind of traditional subcloning where you excise a DNA sequence of interest from one plasmid using restriction enzymes and put them into another plasmid having complementary restriction sites, correct?

A That's correct.

Q And in certain circumstances, the first vector would be what might be called a cloning vector which was unable to express the gene of interest, correct?

A Yes, that's one example.

Q And one of the purposes for wanting to subclone this gene of interest from that cloning vector is to put

it into what we call an expression vector so that the gene of interest would be juxtaposed in proper reading frame with a promoter, correct?

A That is correct.

Q And therefore that would allow for the expression in the host cell under the right conditions of the gene of interest, correct?

A Yes.

Q And so is it fair to say that the -- do you understand the word "novelty" as it --

A I have an understanding of it, yes.

Q Okay. Well, for the sake of getting past the point, would it be fair to say that the novelty of your system was not that it had new elements, but that these elements were arranged in a way that had not been previously arranged to achieve the result which you achieved?

A Yes.

Q Now, you filed a patent application on which you consider to be your invention, correct?

A That is correct.

MR. LABGOLD: And I apologize. I did not, as I was handing out all those extra copies, one of the reasons was I was supposed to have an extra copy for today. Do you have yesterday's exhibits?

CAUSE NO. 2001-61352

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Vs.	(	
CLONTECH LABORATORIES, INC.	(	HARRIS COUNTY, T E X A S
VS.	(	
INVITROGEN CORPORATION	(	133RD JUDICIAL DISTRICT

****

ORAL DEPOSITION OF
KENNETH N. KREUZER, Ph.D.
MARCH 25, 2003

****

EXHIBITS BOUND SEPARATELY

Reported by: LINDA RAYBURN
Job No. 40429

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ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D., produced as a witness at the instance of the DEFENDANT/COUNTERCLAIM PLAINTIFF, and duly sworn, was taken in the above-styled and numbered cause on MARCH 25, 2003, from 10:00 a.m. to 2:22 p.m., before Linda Rayburn, CSR in and for the State of Texas, reported at the offices of Vinson & Elkins, 1001 Fannin Street, Suite 2300, Houston, Texas, pursuant to the Texas Rules of Civil Procedure and the provisions stated in the record or attached hereto.

A P P E A R A N C E S

FOR THE PLAINTIFF/COUNTERCLAIM DEFENDANT:

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MR. MARC R. LABGOLD
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* * * * *

to "donor vector," which we see down a little further on the page?

A Sure.

Q And one last question and we'll take our break. Your definition of "donor vector," is that concept there something which was invented by Dr. Stephen Elledge?

A I think it would be the same answer as before.

MR. LABGOLD: Why don't we go ahead and take a quick break.

(A recess was taken.)

Q (By Mr. Labgold) Back to our Glossary of Terms, I assume you will agree with me that Dr. Elledge did not invent the concept of antibiotics?

A Certainly.

Q And you also agree that he did not invent the idea of using antibiotic resistant genes as selection markers?

A Yes.

Q Conditional origin of replication, is that a concept which was invented by Dr. Elledge?

A No.

Q Do you know if it was published in the art before the development of the Univector system?

A Sure.

Q And do you know if its use in cloning

technologies was discussed in the literature prior to the Elledge Univector development?

A Yes.

Q Are you aware -- pardon me?

A It's used in a variety of situations.

Q Are you aware that Dr. Elledge received certain bacterial strains from a Dr. Barry Wanner at Purdue?

A Yes.

Q And are you aware of the fact that Dr. Elledge provided those strains to Clontech without advising Dr. Wanner of that fact beforehand?

MR. BLANKE: Objection, form.

THE WITNESS: I don't know what the communication was between Dr. Elledge and Dr. Wanner.

Q (By Mr. Labgold) Have you seen that allegation in the record?

A The allegation that it was provided without proper communication?

Q Yes.

A I think I have, yes.

Q Have you seen -- I believe in your report you indicated that you've seen all of the documents that have been produced by both parties; is that correct?

A As far as I know. I came to Austin and was presented with what was thirteen or fifteen boxes of

with licensing.

Q That there was a third-party that had certain rights to the GST fusion purification system? That's what the concern was?

A That's my recollection.

Q And from your review of the documents, Clontech was cognizant of the fact that they did not want to use someone else's technology?

A Hang on a minute. I could be wrong, but that's my recollection at the moment.

Q And Dr. Elledge did not invent GST fusion proteins, correct?

A No.

Q That's correct or not correct?

A Oh, sorry. Dr. Elledge did not invent GST fusion proteins as a general entity, yes.

Q And he did not invent the concept of creating a GST fusion so that the protein to which the GST was fused could be purified, correct?

A That's correct.

Q And in fact, the publication, itself, makes reference to that and being in the prior art, correct?

A Yes.

Q Did you review the correspondence between Clontech and Dr. Elledge concern Clontech's efforts to

(Discussion off the record.)

Q (By Mr. Labgold) I would like to mark as Kreuzer Exhibit 3 a publication in Gene, the journal Gene, G-e-n-e, Volume 150, 1994, Pages 51 to 56, entitled, "Escherichia coli genome targeting, I. Cre-lox-mediated in vitro generation of ori minus plasmids and their in vivo chromosomal integration and retrieval."

(Kreuzer Deposition Exhibit No. 2 was marked for identification.)

MR. LABGOLD: Back on the record here. We have misidentified it. This article, Hasan, et al., from Dr. Szybalski's lab will be Exhibit 2.

Q (By Mr. Labgold) If you'd take a moment to look at this article and tell me if you've seen this before?

A I believe I've seen a related paper. It may be -- maybe it's number two in the series. I'm not sure I've seen this one.

Q And do you understand this as being -- where it says Cre-lox-mediated, this is the same type of Cre-lox recombination that we're talking about, correct?

A That would be -- the reaction, itself, would be the same kind of reaction, yes.

Q And do you understand that this is a -- a

method for inserting genes of interest into an acceptor molecule, in this case a chromosome?

A Again, I would need some time to read through the paper carefully, but it seems -- seems like that's what the title and abstract are, just guessing.

Q And to the extent you need to review any of it in detail, please take as much time as you need. Would you agree that the article describes putting a gene of interest onto a -- a plasmid -- well, let's take a look at Figure 1.

A Okay.

Q And why don't you take a moment to read the legend to Figure 1.

A Okay.

Q And do you have a general understanding of what's represented by this figure?

A Yes, I think so.

Q And is it your understanding that the top plasmid, the top circle there, pNH64a, is used to -- as a vector for a gene of interest?

A Yes.

Q And that that vector contains the two loxP sites?

A Yes.

Q Which when subjected to the Cre enzyme in vitro

results in a recombination event that yields two plasmids that are shown as pNH64b and pNH64c?

A Yes.

Q Now, what's your understanding of that ori minus notation?

A That's a circular fragment of DNA that will go on to insert into bacterial chromosome.

Q And by it being ori minus, that means that that plasmid cannot propagate in a host organism, correct?

A At least not a wild type host organism.

Q And that ori minus feature is used as a selection for the desired reaction, correct?

A Yes, it's used as a negative selection for the desired reaction. Not the reaction that's shown here.

Q Correct.

A The reaction that occurs later.

Q And if I understand what is intended to happen next is that the result of the in vitro recombination with Cre -- oh, and let me ask you this, backing up a step. You've described in your expert report that this Cre-mediated reaction is a reversible reaction, correct?

A Yes.

Q So that where it shows an arrow coming from the big plasmid on the top of Figure 1 of Kreuzer Exhibit 2, down to the two daughter plasmids, that's actually -- it

should be a two-way arrow, correct?

A Yes.

Q And that I believe -- and I apologize, because I don't know exactly where the citation is in your -- oh, I believe if you go to Page 21, I'm sorry, you state that after the two -- do you see about halfway down Page 45?

A Yes.

Q "After the two have been mixed together in the presence of Cre, you will have a mixture of vectors. Because the Cre reaction is reversible, vectors will be fusing and separating in the test tube until you stop the reaction."

A Yes.

Q And so that type of reversible equilibrium is actually going on in this reaction, too, correct?

A Yes, I mean, as I indicated in the report, depending on the DNA concentration, you can push it one way or the other.

Q And what's not shown in Figure 1 of Kreuzer Exhibit 2 is that you then transform this into a host organism, correct?

A Correct.

Q And then the chromosome of that host organism works as an acceptor molecule, if you will, for

Q And by that system, you have a selection mechanism so that you can select for a resulting organism that displays the gene of interest and you will know by the means of the selection that you've got the right mutagenized product, correct?

A You would certainly want to confirm it, but you would -- if the system works properly, you would have that, yes. And again, I haven't looked past Figure 1, so I'm assuming the system works by the lambda recombination. Right. And that's clearly indicated in the abstract.

Q Uh-huh. Now, if Dr. Elledge was aware of this paper before the development of the Univector system, would the ethic provide that he should cite this reference in his article?

A I don't particularly see why at the moment. I don't think his system is built on this at all.

Q Even though it uses several of the key elements here?

A As you pointed out before, there were quite a number of papers that use lox-mediated recombination in a variety of situations.

Q And this one actually goes through taking a gene of interest, putting it into a plasmid, creating a, you know, donor plasmid, if you will, in the ori minus?

A The words "donor" and "acceptor" don't mean very much. The heart of the Elledge system, you know, as I indicated, is the ability to make novel gene combinations, gene fusions, promoter gene constructs. And, you know, other people, as I said before, have used lox sites, for example, to introduce mutations into mouse gene targeting. Those are interesting other applications of lox recombination, but I don't think that the Elledge system is built on any of those, you know, as far as I can see.

Q Uh-huh. Would you agree that the insertion of the gene of interest, the recombination event in Kreuzer Exhibit 2 into the chromosome is also a reversible reaction?

A I don't believe that it is in the cells that they use. Int is -- only refers to when another protein is present, and I doubt if they have that protein present in the cells. But I would have to look at the materials and methods to determine that.

Q And what's the enzyme, the protein that you are referring to?

A XIS, X-I-S. I would -- again, I would have to look over it carefully. The normal -- let me clarify. The normal lambda integration which uses -- in the case of the Int protein, the two sites are different, they

are not the same as with the Cre-lox system. And the normal reaction which occurs between the two different sites goes in one direction with Ints and requires an XIS for the reverse direction.

I would have to look over this more carefully to see. It looks to me like they are using the normal bacterial -- they are using the normal combination of two sites, and so my presumption, if that is true, is that it would require a second protein.

Q If you'd take a look at Page 55, Subsection D.

A Okay.

Q And take as much time as you need to read that section and just --

MR. BLANKE: We're on Exhibit 2 of the Kreuzer deposition?

MR. LABGOLD: Yes, sir. I'm sorry, Kreuzer Exhibit 2 at Page 55. And it's in bold, Subsection D on the left-hand column.

THE WITNESS: Okay. Yes.

Q (By Mr. Labgold) Doesn't this indicate that the inserted gene product can actually be retrieved from the chromosome?

A By introducing the excising protein.

Q Now, if you go to Page 22 of your report, which is Kreuzer Exhibit 1, at the top of the page, you have a

c: Glenn A. Ballard, Jr. (*by fax*)
Tracey B. Davies [*Firm*]
M. Michelle Muller [*Firm*]
Jason M. Powers [*Firm*]

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FACSIMILE TRANSMITTAL PAGE

DATE: May 2, 2003

TO: Glenn A. Ballard, Jr.
Bracewell & Patterson

FAX: 713.221.1212

PHONE: 713.223.2900

TO: Richard J. Oparil
Patton Boggs (DC)

FAX: 202.457.6315

PHONE: 202.457.6000

PAGES: 5 (including this transmittal page)

CLIENT/MATTER: INV850/13000

FROM: David P. Blanke

MESSAGE: **David Blanke's 05/02/03 letter to Oparil re agreements to narrow issues in Clontech's motion to compel discovery from Baylor.**

Hard Copy Follows: ☐ Yes ☒ No

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May 6, 2003

By Fax

Mr. Richard J. Oparil
Patton Boggs L.L.P.
2550 M Street NW
Washington, DC 20037

Re: *Baylor College of Medicine, et al. v. Clontech Laboratories, Inc.*;
Cause No. 2001-61352

Dear Richard:

I am further responding to your April 14 letter. Earlier I wrote regarding the Ruobo Zhang exhibits. As to the '808 continuations, we will be producing the non-privileged documents on this issue. In the meantime, I am providing the accompanying preliminary amendment and notice of allowance from the PTO.

Very truly yours,

David P. Blanke

attachment
c: Glenn A. Ballard, Jr. (*by fax; w/att.*)
Kevin Bell (*by fax; w/att.*)
Tracey B. Davies [*Firm; w/o att.*]
M. Michelle Muller [*Firm; w/o att.*]
Jason M. Powers [*Firm; w/o att.*]

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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Washington, D.C. 20231

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER
	47

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

--See attached--

Notice of Allowability	Application No. 09/122,384	Applicant(s) ELLEDGE ET AL.	
	Examiner James S. Ketter	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--
I claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

- ☒ This communication is responsive to the amendment of 10/3/02 and the IDS of 3/4/03.
- ☒ The allowed claim(s) is/are 43-68.
- ☒ The drawings filed on 20 March 2001 are accepted by the Examiner.
- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All b) ☐ Some* c) ☐ None of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. _____.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - * Certified copies not received: _____.
- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - (a) ☐ The translation of the foreign language provisional application has been received.
- ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

pplicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted elow. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

- ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF FORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

- ☐ CORRECTED DRAWINGS must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached 1) ☐ hereto or 2) ☐ to Paper No. _____.
  - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
  - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

- ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the ttached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

ttachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statements (PTO-1449), Paper No. 30, 32 & 45.
- ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
- 2☐ Notice of Informal Patent Application (PTO-152)
- 4☐ Interview Summary (PTO-413), Paper No._____.
- 6☐ Examiner's Amendment/Comment
- 8☐ Examiner's Statement of Reasons for Allowance
- 9☐ Other

JAMES KETTER
PRIMARY EXAMINER

UNITED STATES PATENT AND TRADEMARK OFFICE

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NOTICE OF ALLOWANCE AND FEE(S) DUE

21586 7590 04/22/2003

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EXAMINER	
KETTER, JAMES S	
ART UNIT	CLASS-SUBCLASS
1636	435-006000

DATE MAILED: 04/22/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1300	$0	$1300	07/22/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE
Commissioner for Patents
Washington, D.C. 20231
Fax (703)746-4000

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use label)

21586 7590 04/22/2003

VINSON & ELKINS, L.L.P.
1001 FANNIN STREET
2300 FIRST CITY TOWER
HOUSTON, TX 77002-6760

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN I. ELLEDGE	BAY136/4-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1300	$0	$1300	07/22/2003

EXAMINER	ART UNIT	CLASS-SUBCLASS
KETTER, JAMES S	1636	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) ☐ individual ☐ corporation or other private group entity ☐ government

4a. The following fee(s) are enclosed:

☐ Issue Fee
☐ Publication Fee
☐ Advance Order - # of Copies _____

4b. Payment of Fee(s):

☐ A check in the amount of the fee(s) is enclosed.
☐ Payment by credit card. Form PTO-2038 is attached.
☐ The Commissioner is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

Commissioner for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

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NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

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United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY136/4-010CIP	4340

21586 7590 04/22/2003

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EXAMINER	
KETTER, JAMES S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/22/2003

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The patent term adjustment to date is 0 days. If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the term adjustment will be 0 days.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (http://pair.uspto.gov)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY136/4-010CIP	4340

21586 7590 04/22/2003

VINSON & ELKINS, L.L.P.
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UNITED STATES

EXAMINER	
KETTER, JAMES S	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/22/2003

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003: Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: http://www.uspto.gov/main/howtofees.htm.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Vinson&Elkins V&E
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Timothy S. Corder
Direct Dial 512-542-8446
Direct Fax 512-236-3377
tcorder@velaw.com

October 3, 2002

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002 — Timothy S. Corder
Date

Assistant Commissioner for Patents
Washington, D.C. 20231

Re: U.S. Patent Application SN 09/122,384 "Rapid Subcloning Using Site-Specific Recombination," by Elledge et al.
Attorney Docket No.: BAY136/4-010CIP/36000; Client Ref.: OTA # 97-27
Confirmation No. 4340

Sir:

Enclosed for filing in the above-referenced patent application is a Preliminary Amendment for filing in the above-referenced patent application.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to appropriately deduct or credit the requisite amount from Vinson & Elkins L.L.P. deposit account No. 22-0365/BAY136/4-010CIP/36000.

Respectfully submitted,

Timothy S. Corder
Reg. No. 38,414

9282:5588

Enclosure

311728_1.DOC

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Stephen J. Elledge et al.	Group Art Unit: 1636
Serial No.: 09/122,384	Examiner: J. Ketter
Filed: July 24, 1998	Atty. Dkt. No.: BAY136/4-10CIP/36000
For: Rapid Subcloning Using Site-Specific Recombination	Confirmation No. 4340

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002 — Timothy S. Corder

PRELIMINARY AMENDMENT

VIA FACSIMILE NO. 703-746-5155

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, the Examiner is requested to please amend the above-captioned application as follows:

AMENDMENT

A. **In the Claims:**

Please cancel all pending claims, i.e. claims 1-20, 26, 30-35, and 37-42, and enter the following new claims:

43. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

44. The composition of claim 43, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

45. The composition of claim 43, wherein the composition comprises an enzyme activity with a Cre recombinase efficiency of about 16.8% per microgram of protein.

46. An isolated nucleic acid molecule comprising a coding region wherein the coding region encodes a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

47. The nucleic acid molecule of claim 46, wherein the coding region comprises the nucleic acid sequence of SEQ ID NO:10.

48. The nucleic acid molecule of claim 46, wherein the isolated nucleic acid molecule is an expression vector.

49. The nucleic acid molecule of claim 46, wherein the coding region is operatively linked to a promoter effective to direct expression of a glutathione-S-transferase-Cre recombinase fusion polypeptide.

50. The nucleic acid molecule of claim 49, wherein the promoter is an inducible promoter.

51. The nucleic acid of claim 50, wherein the promoter is the *tac* promoter.

52. A host cell comprising the nucleic acid molecule of claim 46.

53. A host cell comprising the nucleic acid molecule of claim 49.

54. The host cell of claim 53, wherein the host cell expresses a Cre recombinase activity.

55. The host cell of claim 53, further defined as an E. coli cell.

56. A bacterial cell engineered to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

57. The bacterial cell of claim 56, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

58. A method of producing a glutathione-S-transferase-Cre-recombinase fusion polypeptide comprising:

obtaining an expression vector comprising a coding region encoding a glutathione-S-transferase-Cre-recombinase fusion polypeptide operatively linked to a promoter;

transforming or transfecting the vector into a cell; and

growing the cell under conditions effective to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

59. The method of claim 58, further comprising isolating the glutathione-S-transferase-Cre-recombinase fusion polypeptide.

60. The method of claim 59, wherein isolating the polypeptide comprises glutathione affinity chromatography.

61. A method of recombining nucleic acid segments, wherein each segment comprises a *lox* site specific recombinase site, the method comprising contacting the nucleic acid segments with a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

62. The method of claim 61, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

63. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide and one or more nucleic acid molecules, wherein the nucleic acids comprise a site specific recombinase site.

64. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a lox recombination site upstream in a 5' to 3' orientation from an amino acid encoding region.

65. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a transcription regulatory element upstream in a 5' to 3' orientation of a lox recombinase site.

66. The composition of claim 64 wherein the lox recombinase site is a *lox*P, *lox*P2, *lox*P3, *lox*P23, *lox*P511, *lox*B, *lox*C2, *lox*L, *lox*R, *lox*Δ86, *lox*Δ117, or *lox*H site.

67. The composition of claim 65 wherein the lox recombinase site is a *lox*P, *lox*P2, *lox*P3, *lox*P23, *lox*P511, *lox*B, *lox*C2, *lox*L, *lox*R, *lox*Δ86, *lox*Δ117, or *lox*H site.

68. The composition of claim 64, wherein the amino acid encoding region is a member of a nucleic acid library.

II. REMARKS

The claims in this preliminary amendment do not add new matter to the application and their entry is therefore respectfully requested. Support for the claims may be found throughout the Specification and at least in Example 3 found on page 47.

IV. CONCLUSION

Applicants respectfully submit that the present application and all claims are in condition for immediate allowance and early notice to such effect is earnestly solicited. If, in the opinion of the Examiner, a phone call may help expedite prosecution of this application, the Examiner is invited to contact the undersigned representative at (512) 542-8446.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Vinson & Elkins L.L.P. Deposit Account No. 22-0365/BAY136/4-10CIP/36000.

Respectfully submitted,

Timothy S. Corder
Reg. No. 38,414
Agent for Applicant

Vinson & Elkins L.L.P.
2300 First City Tower
1001 Fannin
Houston, Texas 77002-6760
512/542-8446

Date: October 3, 2002

Vinson&Elkins V&E
ATTORNEYS AT LAW

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5 MAY -6 P1:59

David P. Blanke
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Direct Fax (512) 236-3314
dblanke@velaw.com

FACSIMILE TRANSMITTAL PAGE

DATE: May 6, 2003

	Glenn A. Ballard, Jr. Bracewell & Patterson	**FAX:** PHONE:	**713.221.1212** 713.223.2900
TO:	Marc Labgold Kevin M. Bell Patton Boggs (VA)	**FAX:** PHONE:	**703.744.8001** 703.744.8000
TO:	Richard J. Oparil Patton Boggs (DC)	**FAX:** PHONE:	**202.457.6315** 202.457.6000
PAGES:	14 (including this transmittal page)	CLIENT/MATTER:	INV850/13000
FROM:	David P. Blanke		

MESSAGE: **David Blanke's 05/06/03 letter further responding to 04/14/03 Oparil letter.**

Hard Copy Follows ☐ Yes ☒ No

PATTON BOGGS LLP
ATTORNEYS AT LAW

2550 M Street NW
Washington DC 20037
(202) 457-6000

Facsimile (202) 457-6315

To:	**Amy Bell**
Company:	**Patton Boggs LLP**
Fax Number:	**703.744.8001**
Phone Number:	**703.744.8000**
Total Pages Including Cover:	**15**
From:	**Richard Oparil**
Sender's Direct Line:	202.457.6496
Date:	May 6, 2003
Client Number:	020187.0102

Comments:

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dblanke@velaw.com

5 MAY -6 P1:59

FACSIMILE TRANSMITTAL PAGE

DATE:	May 6, 2003		
	Glenn A. Ballard, Jr. Bracewell & Patterson	FAX: PHONE:	713.221.1212 713.223.2900
TO:	Marc Labgold Kevin M. Bell Patton Boggs (VA)	FAX: PHONE:	703.744.8001 703.744.8000
TO:	Richard J. Oparil Patton Boggs (DC)	FAX: PHONE:	202.457.6315 202.457.6000
PAGES:	14 (including this transmittal page)	CLIENT/MATTER:	INV850/13000
FROM:	David P. Blanke		

MESSAGE: **David Blanke's 05/06/03 letter further responding to 04/14/03 Oparil letter.**

Hard Copy Follows ☐ Yes ☒ No

Vinson&Elkins V&E
ATTORNEYS AT LAW

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dblanke@velaw.com

May 6, 2003

By Fax

Mr. Richard J. Oparil
Patton Boggs L.L.P.
2550 M Street NW
Washington, DC 20037

Re: *Baylor College of Medicine, et al. v. Clontech Laboratories, Inc.*;
Cause No. 2001-61352

Dear Richard:

I am further responding to your April 14 letter. Earlier I wrote regarding the Ruobo Zhang exhibits. As to the '808 continuations, we will be producing the non-privileged documents on this issue. In the meantime, I am providing the accompanying preliminary amendment and notice of allowance from the PTO.

Very truly yours,

David P. Blanke

attachment
c: Glenn A. Ballard, Jr. (*by fax; w/att.*)
Kevin Bell (*by fax; w/att.*)
Tracey B. Davies [*Firm; w/o att.*]
M. Michelle Muller [*Firm; w/o att.*]
Jason M. Powers [*Firm; w/o att.*]

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER
	47

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

--See attached--

Notice of Allowability	Application No. 09/122,384	Applicant(s) ELLEDGE ET AL.	
	Examiner James S. Ketter	Art Unit 1636	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address*--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment of 10/3/02 and the IDS of 3/4/03*.
2. ☒ The allowed claim(s) is/are *43-68*.
3. ☒ The drawings filed on *20 March 2001* are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____.
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. _____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Informal Patent Application (PTO-152)
3☒ Information Disclosure Statements (PTO-1449), Paper No. 10, 12 & 17.
4☐ Interview Summary (PTO-413), Paper No. _____.
5☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
6☐ Examiner's Amendment/Comment
7☐ Examiner's Statement of Reasons for Allowance
8☐ Other

JAMES KETTER
PRIMARY EXAMINER

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
ADDRESS: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

NOTICE OF ALLOWANCE AND FEE(S) DUE

21586 7590 04/22/2003

VINSON & ELKINS, L.L.P.
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HOUSTON, TX 77002-6760

EXAMINER	
KETTER, JAMES S	
ART UNIT	CLASS-SUBCLASS
1636	435-006000

DATE MAILED: 04/22/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1300	$0	$1300	07/22/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (REV. 04-02) Approved for use through 01/31/2004.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE
Commissioner for Patents
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31586 7590 04/22/2003

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(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN I. ELLEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION .

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1300	$0	$1300	07/22/2003

EXAMINER	ART UNIT	CLASS-SUBCLASS
KETTER, JAMES S	1636	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-01CIP	6340

21186 7590 04/22/2003

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EXAMINER	
KETTER, JAMES S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/22/2003

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The patent term adjustment to date is 0 days. If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the term adjustment will be 0 days.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (http://pair.uspto.gov)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010C1P	4340

EXAMINER	
KETTER, JAMES S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/22/2003

21586 7590 04/22/2003

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UNITED STATES

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003: Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: http://www.uspto.gov/main/howtofees.htm.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

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October 3, 2002

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002 — Timothy S. Corder
Date

Assistant Commissioner for Patents
Washington, D.C. 20231

Re: *U.S. Patent Application SN 09/122,384 "Rapid Subcloning Using Site-Specific Recombination," by Elledge et al.*
Attorney Docket No.: BAY136/4-010CIP/36000; Client Ref.: OTA # 97-27
Confirmation No. 4340

Sir:

Enclosed for filing in the above-referenced patent application is a Preliminary Amendment for filing in the above-referenced patent application.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to appropriately deduct or credit the requisite amount from Vinson & Elkins L.L.P. deposit account No. 22-0365/BAY136/4-010CIP/36000.

Respectfully submitted,

Timothy S. Corder
Reg. No. 38,414

9282:5588

Enclosure

311728_1.DOC

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Stephen J. Elledge et al.	Group Art Unit: 1636
Serial No.: 09/122,384	Examiner: J. Ketter
Filed: July 24, 1998	Atty. Dkt. No.: BAY136/4-10CIP/36000
For: Rapid Subcloning Using Site-Specific Recombination	Confirmation No. 4340

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002 — Timothy S. Corder

PRELIMINARY AMENDMENT

VIA FACSIMILE NO. 703-746-5155

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, the Examiner is requested to please amend the above-captioned application as follows:

AMENDMENT

A. In the Claims:

Please cancel all pending claims, i.e. claims 1-20, 26, 30-35, and 37-42, and enter the following new claims:

43. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

44. The composition of claim 43, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

45. The composition of claim 43, wherein the composition comprises an enzyme activity with a Cre recombinase efficiency of about 16.8% per microgram of protein.

46. An isolated nucleic acid molecule comprising a coding region wherein the coding region encodes a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

47. The nucleic acid molecule of claim 46, wherein the coding region comprises the nucleic acid sequence of SEQ ID NO:10.

48. The nucleic acid molecule of claim 46, wherein the isolated nucleic acid molecule is an expression vector.

49. The nucleic acid molecule of claim 46, wherein the coding region is operatively linked to a promoter effective to direct expression of a glutathione-S-transferase-Cre recombinase fusion polypeptide.

50. The nucleic acid molecule of claim 49, wherein the promoter is an inducible promoter.

51. The nucleic acid of claim 50, wherein the promoter is the *tac* promoter.

52. A host cell comprising the nucleic acid molecule of claim 46.

53. A host cell comprising the nucleic acid molecule of claim 49.

54. The host cell of claim 53, wherein the host cell expresses a Cre recombinase activity.

55. The host cell of claim 53, further defined as an E. coli cell.

56. A bacterial cell engineered to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

57. The bacterial cell of claim 56, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

58. A method of producing a glutathione-S-transferase-Cre-recombinase fusion polypeptide comprising:

obtaining an expression vector comprising a coding region encoding a glutathione-S-transferase-Cre-recombinase fusion polypeptide operatively linked to a promoter;

transforming or transfecting the vector into a cell; and

growing the cell under conditions effective to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

59. The method of claim 58, further comprising isolating the glutathione-S-transferase-Cre-recombinase fusion polypeptide.

60. The method of claim 59, wherein isolating the polypeptide comprises glutathione affinity chromatography.

61. A method of recombining nucleic acid segments, wherein each segment comprises a *lox* site specific recombinase site, the method comprising contacting the nucleic acid segments with a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

62. The method of claim 61, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

63. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide and one or more nucleic acid molecules, wherein the nucleic acids comprise a site specific recombinase site.

64. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a lox recombination site upstream in a 5' to 3' orientation from an amino acid encoding region.

65. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a transcription regulatory element upstream in a 5' to 3' orientation of a lox recombinase site.

66. The composition of claim 64 wherein the lox recombinase site is a *lox*P, *lox*P2, *lox*P3, *lox*P23, *lox*P511, *lox*B, *lox*C2, *lox*L, *lox*R, *lox*Δ86, *lox*Δ117, or *lox*H site.

67. The composition of claim 65 wherein the lox recombinase site is a *lox*P, *lox*P2, *lox*P3, *lox*P23, *lox*P511, *lox*B, *lox*C2, *lox*L, *lox*R, *lox*Δ86, *lox*Δ117, or *lox*H site.

68. The composition of claim 64, wherein the amino acid encoding region is a member of a nucleic acid library.

II. REMARKS

The claims in this preliminary amendment do not add new matter to the application and their entry is therefore respectfully requested. Support for the claims may be found throughout the Specification and at least in Example 3 found on page 47.

IV. CONCLUSION

Applicants respectfully submit that the present application and all claims are in condition for immediate allowance and early notice to such effect is earnestly solicited. If, in the opinion of the Examiner, a phone call may help expedite prosecution of this application, the Examiner is invited to contact the undersigned representative at (512) 542-8446.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Vinson & Elkins L.L.P. Deposit Account No. 22-0365/BAY136/4-10CIP/36000.

Respectfully submitted,

Timothy S. Corder
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Agent for Applicant

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Date: October 3, 2002

P18
STIPX
PRDSX

CAUSE NO. 2001-61352

BAYLOR COLLEGE OF MEDICINE and BCM TECHNOLOGIES, INC.,	§	IN THE DISTRICT COURT
PLAINTIFFS/COUNTERCLAIM DEFENDANTS,	§	
v.	§	HARRIS COUNTY, TEXAS
CLONTECH LABORATORIES, INC.,	§	
DEFENDANT/COUNTERCLAIM PLAINTIFF,	§	133RD JUDICIAL DISTRICT
INVITROGEN CORPORATION,	§	
ADDITIONAL COUNTERCLAIM DEFENDANT,	§	

FILED
CHARLES BACARISSE
District Clerk
OCT 29 2002
Harris County, Texas
By Deputy

STIPULATED PROTECTIVE ORDER

Whereas pretrial discovery in this action will necessarily involve the disclosure of trade secrets or confidential research, development, or commercial information of both parties and of non-parties from whom discovery may be sought; and

Whereas the parties have in good faith conferred and have agreed upon the terms of a Protective Order and for good cause shown; therefore

The parties stipulate, pursuant to Texas Rule of Civil Procedure 192.6, subject to the approval of the Court, to the following Protective Order:

1. **Scope of Protection.**

1.1 This Protective Order shall govern any record of information, designated pursuant to ¶ 2 of this Protective Order, produced in this action, including all designated deposition testimony, all designated testimony taken at a hearing or other proceeding, interrogatory answers, documents and